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Serial No. 09/926,167

REMARKS

Reconsideration of this application is requested. Claims 1-24 were pending in the case. However, the claims have been amended as noted herein. Claims 1-23 and 36-43 are now pending in the case.

Claims 1-24 (now claims 1-23 were amended as noted in item III below.

Claims 36 - 43 were added. Claims 36-42 are directed specifically to the hemoglobin-trolox conjugate and is supported by the specification as originally filed.

Support for claim 42 can be found in Table 2 of the application.

Support for claim 43 can be found at page 26, line 1.

I. PRIORITY

With regard to the Examiner's note that no claim to priority was made in Declaration in accordance with 35 U.S. C. 119 (a) - (d), please note that Applicant has amended page 1 of the application to make reference to the priority document. Also, please note that reference and claim to the priority was made in the Application data sheet filed at the time of National phase entry with the application and in the National Phase entry cover sheet to the Commissioner of Patents and Trademarks executed on September 17, 2001.

II. DRAWINGS

We make note of the Examiner's rejections of the drawings and his statement that formal drawings will be required when the application is allowed. Applicant will attend to the drawing requirements accordingly.

II. CLAIM OBJECTIONS

The typographical error in claim 7 and the multiple dependent claims have been attended to. The claims have been amended to conform to United States practice. More particularly, "R₁" at

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line 9 of claim 7 was replaced with "R". Further the multiple dependent claims, claims 5, 15-17, 20 and 24 have been amended in accordance with United States practice.

III. CLAIM REJECTIONS - 35 U.S.C § 112

The Examiner rejected claims 1-4 and 7 as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to make, and/or use the invention. The Examiner has stated that the claims are directed to any biocompatible chemical composition having oxygen transporting capabilities chemically bound to one or more biocompatible antioxidants. However, the Examiner has stated that only hemoglobin conjugates have been disclosed. Although, applicant does not necessarily agree with the Examiner, Applicant has amended the claims to be directed to hemoglobin-based conjugates and reserves the right to pursue any other aspects of the invention in a further continuation or continuation-in-part application. No amendment is to be construed as a basis to deny any right to invoke the doctrine of equivalents in construction of any allowed claims.

The Examiner also stated that the examples provided are to Hemoglobin c- 2,5,7, 8-tetramethyle 2-carboxylchroman-6-ol (Trolox) or polOR-HB-TX conjugates. Claims to these specific conjugates have been retained in the application.

Claims 11 - 23 have also been rejected by the Examiner under 35 U.S.C. 112, second paragraph as being indefinite or failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The Examiner states that there is insufficient antecedent basis for R4 and R1 in claim 11, R1, R2, R3 in Claim 22 and R4 in claim 23. Applicant has amended claim 11 to overcome the Examiner's rejections, by correcting the typographical error by replacing "R₁" with "R₄" at the second to last line of the claim. This should also overcome the rejection to claim 23. Claim 22 was amended by replacing R₁ R₂, and R₃ with R'₁, R'₂ and R'₃ to conform to the nomenclature of claim 11 and provide proper antecedent basis.

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Further the Examiner stated that he does not understand the term "direct bond" as a definition of "R₄". Please note that it is submitted that it would be clear to a person skilled in the art that if R₄ is a direct bond the "COOH" would be directly bonded to the chroman structure (i.e. R₄ is nothing), alternatively, R₄ can be a C₁₋₈ alkyl chain.

IV CLAIM REJECTIONS 35 USC § 102

The Examiner rejected claims 1 - 17 on the basis of Adamson et al. (WO 99/56723), however this reference was published after the priority date of the present application and within one year of the PCT filing date and is the inventor's own publication and is commonly owned with the present application.

The Examiner rejected claims 1-3, 5-6, 13-15 and 20 as being anticipated by Kluger (WO 97/00236), on the basis that Kluger teaches a hemoglobin-biomolecule conjugate wherein hemoglobin-biomolecule conjugate is bonded to the crosslinking reagent 3,5,3''5''-bipheyltetracarbonyl tetrakis (3,5-dibromosalicylate) and wherein the biomolecule conjugate, norepinephrine and epinephrine falls within the wordings of "non-enzymatic phenolic compounds". Applicant respectfully traverses this objection. With regard to the Examiner's rejection of the claims as being anticipated by WO/97/00236 by Kluger et. al. Applicant cannot agree. Kluger et al, describe the use of a hemoglobin linker that has two or more reaction sites available for further chemical reactions. There is no specific mention in Kluger of using the cross-linker to link antioxidants *per se* to hemoglobin with the said activity, purpose and result of the present invention. Further, Applicant submits that the compounds mentioned in Kluger are not generally known by a person skilled in the art to be used as an antioxidant. On the other hand, the claims of the present invention are limited to "antioxidants". Further it is submitted that Kluger does not teach a hemoglobin conjugate having an antioxidant and wherein the hemoglobin retains its oxygen transport capabilities. Also, Kluger does not teach directly linking an antioxidant or other compound to the hemoglobin (e.g. not through an intramolecular crosslinker).

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V. CLAIM REJECTIONS 35 USC § 103

The Examiner rejected claims 4, 7-12, 16-19, 21-24 as being obvious in light of Hsia (US 5789376) and Beach et al. (Archives of Biochemistry and Biophysics 1992 abstract, 297 (2), 258-64). Applicant respectfully traverses this rejection.

Although Trolox was a known antioxidant, Applicant cannot agree that it would have been obvious to conjugate it with Hemoglobin to obtain an antioxidant to obtain the result of the present invention. First Hsia does not disclose a hemoglobin conjugated to an antioxidant of the present invention, a "phenolic" antioxidant. Nor does Hsia suggest that any other anti-oxidants should be used or that by binding an antioxidant to the hemoglobin one obtains a synergistic effect. [For example see pages 19, line 28 and page 26, Example 9 of the present application.] Further nowhere, does Beech suggest to bind the TROLOX to hemoglobin to ameliorate its antioxidant activity. As such it is respectfully submitted that one of ordinary skill could not have combined Hsia with Beech to get a conjugate that both transports oxygen and that can ameliorate antioxidant activity of a bound antioxidant. As such it is respectfully submitted that it would not have been obvious to combine the teachings of Hsia and Beech to obtain the present invention.

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Applicant respectfully requests that a timely Notice of Allowance be issued in this case.
Should the Examiner deem it beneficial to discuss the application in greater detail, he is kindly
requested to contact Anita Nador by telephone at (416) 957-1684 at his convenience.

Respectfully submitted,
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Attachment: Figures 1 - 4

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